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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/617,569	07/17/00	ROELVINK	P 204133

023460
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EXAMINER	
FOLEY,S	
ART UNIT	**PAPER NUMBER**
1648	11

DATE MAILED: 08/14/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/617,569	ROELVINK ET AL.	
	Examiner	Art Unit	
	Shanon A. Foley	1648	

-- The MAILING DATE of this communication appears n the c ver sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32 and 40-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32 and 40-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10 ; 12*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-32 and 40-43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is maintained for reasons of record.

This enablement rejection is based on the fact that a CD40 ligand depresses the immune response when delivered by an adenovirus vector for gene therapy, Stein et al. (Gene Therapy 1998; 5: 431-439). Yu et al. (Yu et al. Proceedings of the Association of American Physicians. 1998 Jan-Feb; 110(1):50-64 (abstract) teach that osteopontin has no effect on the humoral immune response and a reduction in T cell activation upon administration. It is concluded that due to the state of the art teaching the negative effects anti-CD40 and osteopontin on the immune system and the lack working examples or guidance in the specification on the predictability of up-regulating the immune response while using the anti-CD40 ligand to target immune effector cells, it is determined that undue experimentation by one skilled in the art would be required to practice the claimed invention.

In response, applicant submits that Toes et al. (Sem. Immunol. 1998; 10: 443-448) demonstrate that the CD40 ligand can be used to prime T cells. Applicant also cites Ashkar et al.

(Science 2000; 287: 860-864) to demonstrate Eta-1 expression is an early step in the pathway that leads to type I immune responses.

Upon review of the references applicant has submitted, it cannot be denied that there is conflicting data about the role of CD40 and osteopontin. This is clear evidence that there is unpredictability in the art as to what effect these compounds have on the immune system when administered. However, the following observation should also be noted. The instant application is drawn to administering a virus expressing CD40 and osteopontin as ligands. The references in the previous Office action show these substances being administered alone to immunologically unaltered rats (Yu et al. abstract) or via a viral vector to immunologically unaltered mice (Stein et al. abstract and "mice" on page 436). Applicant's references are more about studying the function of these substances in immunologically altered mice that are deficient in making these substances (Ashkar et al., abstract and Toes et al. page 445). Since the claims do not specify administering the complex to immunologically altered individuals, the rejection is maintained and it has been made clear that conflict exists in the art in terms of immune response elicited by these components, the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4-7, 9, 11-16, 19, 26, 27, 40, 42, and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Wickham et al. (U.S. Patent 5,846,782) for reasons of record.

Applicant argues that Wickham et al. do not anticipate the claimed invention because the reference does not specifically identify "passenger genes", and states that these may be any number of things, like therapeutic genes, toxins, and prodrugs. Applicant's state that the Office action only asserts that these elements (i.e. HSV thymadine kinase) "***can*** induce a strong immune repsonse", and states that the Office action is trying to establish anticipation by inherency. Applicant cites case law for support that things that ***may*** happen are not enough to establish inherency.

Applicant's arguments have been considered, but are found to be unpersuasive. The ability of inducing an immune response would be an innate property of an immunogenic transgene. This immunogenic characteristic of a specific transgene that is capable of evoking specific immune responses against it could not be derived from another source if it is not present. Therefore, the nature of the immunogenic transgene selected by the skilled artisan would elicit an immune response. The reference does not have to teach the nature of each and every possible passenger gene, since the skilled artisan would know these properties when the selection of the specific immunogenic passenger gene is made. The rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 8 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wickham et al. as applied to claims 1, 2, 4-7, 9, 11-16, 19, 26, 27, 40, 42, and 43 above, and

further in view of Hitt et al. (Methods in Molecular Genetics.1995; 7: 13-30) for reasons of record.

Claims 18, 20-23, 25, 28-30, 32, and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wickham et al. and Hitt et al. as applied to claims 2, 4-16, 19, 26, 27, 32, 40, 42, and 43 above, and further in view of Janeway et al. (Immunobiology. 3rd edition. 1997, Garland Publishing Inc. Page 7:27) for reasons of record.

Applicant argues the references individually and asserts that there is no motivation to combine the teachings of Wickham et al. with the teachings of Hitt et al. drawn to a method of adding multiple genes to an adenovirus genome.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The test of obviousness is not an express suggestion of the claimed invention in any or all references but what references taken together would suggest to those of ordinary skill in the art presumed to be familiar with them.

Furthermore, one of ordinary skill in the art at the time the invention was made would have been motivated to incorporate multiple genes taught by Hitt et al. into the retargeted recombinant adenovirus (taught by Wickham et al.) in order to elicit an immune response against more antigens present in a pathogen. As discussed in the previous action, liposomes are well known in the art to fascilitate binding to a cell surface and would be an obvious choice for the skilled artisan interested in delivering components to a cell surface.

As evidenced by the teachings in the references, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon A. Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on 7:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Laurie Scheiner and James Housel can be reached at (703) 308-1122 and (703) 308-4027, respectively. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley/SAF
August 6, 2001

LAURIE SCHEINER
PRIMARY EXAMINER